Remarks

Claims 170-179 are pending in the subject application. By this Amendment, Applicants have canceled claims 170-179 and added claims 180-304. Support for the new claims can be found throughout the subject specification and in the claims as originally filed (see, for example, specification, pages 8-16, 37-48, 62-64, and Figure 1). Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 180-304 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

In the previous Office Action, the previously pending claims were rejected under 35 U.S.C. §103(a) as being unpatentable over Morris *et al.* in view of Hol *et al.* and Stylli *et al.* The Office Action asserted that Morris *et al.* taught a method to identify the optimal salt form for BMS-180431. The Office Action also asserts that the physiochemical properties of seven salts were studied using a "multi-tier approach" and that at least two of the samples comprise a salt and that at least one of the samples differs from the others. The Office Action also argues that once optimal salts were determined, the compounds were further screened against various excipients and for stability. The Office Action further argues that Morris *et al.* teach analyzing the analysis of the samples by HPLC and UV absorbance.

As the Patent Office is aware, all the claim limitations must be taught or suggested by the prior art to establish the prima facie obviousness of a claimed invention. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (CCPA 1974). In the case of the presently claimed invention, it is respectfully submitted that Morris *et al.* fail to teach a number of the limitations found in the newly presented independent and dependent claims. For example, Morris *et al.* fail to teach preparing an array of at least 96 samples in tubes and support plates or in sample well plates, labeling, identifying, and dispensing components into sample tubes or sample wells with a sample generation module; sealing said samples; processing said samples comprising heating said samples in a sample incubation module to a temperature (T1), analyzing said samples for the presence of undissolved solids using machine vision technology, cooling said samples to a final temperature (T2), wherein at least one of the processed samples comprises a crystalline salt form of the small molecule pharmaceutical; and analyzing the processed array of samples comprising detecting crystalline solid formation in said samples using polarized light and machine vision technology, measuring a property for each crystalline solid and using the results of said measuring to group similar crystalline salt polymorphs,

hydrates and solvates that belong to the same crystal family using informatics. Applicants further submit that the Morris *et al.* fail to teach: sealing said samples with a cap; an array comprising at least 1000 samples; the generation of a work list for instructing an automated distribution mechanism to prepare said array of samples; dispensing of components by a liquid handling system with pipette tips having septum-piercing capability; samples containing less than 1 milligram of said small molecule pharmaceutical; the grouping of samples using Raman spectroscopy; the quenching of the crystallization process by removing solvent from the samples; processing of samples that further comprises adding a non-solvent to said samples; processing of samples that further comprises evaporating solvent from said samples; the piercing of a capped sample and aspirating fluid from the samples; analyzing arrays of samples with a polarized filter apparatus to determine crystal birefringence and distinguish crystalline solids from amorphous solids; the use of a small molecule pharmaceutical that has previously evaded crystallization; the identification of a crystalline salt in processed samples that is an additional polymorph of a small molecule pharmaceutical previously known as a monomorphic compound; analysis of at least one crystal family and any orphan crystals; the addition of nucleation initiators; and/or the grouping of samples into categories selected from the group consisting of: a) samples containing no precipitate; b) samples with a single polymorph; c) samples with a polymorph mixture; d) samples with amorphous forms of said small molecule pharmaceutical; and e) samples with mixtures of categories b-d.

Applicants further submit that Morris does not teach "grouping" as asserted in the Office Action. Morris only has one example of a salt from each family and each of Morris' salts come from a different family. Thus, Morris *et al.* only consider different salt forms and Morris *et al.* fail to teach a number of salt forms within a single family of salt forms. The subject invention, however, provides methods of grouping together salt forms from the same family.

Applicants respectfully submit that Hol *et al.* and Stylli *et al.* fail to cure the deficiencies noted in the teachings of Morris *et al.* It is respectfully submitted that Hol *et al.* do not teach making salt crystals of small molecule pharmaceuticals. Rather, Hol *et al.* teach crystallizing proteins and it is respectfully submitted that the methods of Hol *et al.* will not crystallize small pharmaceutical molecules. Hol *et al.* uses entirely different compositions, conditions, and processing steps than the present invention. Hol et al. is thus, a non-enabling reference. On page 5, line 3, the examiner misconstrues Hol *et al.* by taking words out of context. The deleted words read "especially a

biological macromolecule such as a protein". Hol *et al.* make no specific mention of any type of molecule other than a protein anywhere in the reference and is non-enabling for crystallizing small molecules. Contrary to the assertion on page 5 of the Office Action, Hol *et al.* further do not teach varying the temperature during the crystallization process (see, for example, column 10, about line 60). Hol *et al.* state that the temperature can be optimized (column 11, about line 25); however, Hol *et al.* fail to teach that the temperature can be varied during his process.

Applicants further submit that the deficiencies of Morris *et al.* and Hol *et al.* are not cured by Stylli *et al.* Applicants respectfully submit that Stylli *et al.* is non-analogous art in that Stylli *et al.* teach combinatorial activity assays and measuring the biological activity of different molecules. Stylli *et al.* fail to teach the crystallization of a single molecule. Indeed, Stylli *et al.* do not teach or suggest crystallization of any kind. Thus, it is respectfully submitted that one skilled in the art would not have turned to Stylli *et al.* for any relevant teachings.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

Frank C Eisenschenk

Frank C. Eisenschenk, Ph.D.
Patent Attorney
Registration No. 45,332
Phone No.: 352-375-8100
Fax No.: 352-372-5800
Address: 2421 N.W. 41st Street, Suite A-1
Gainesville, FL 32606-6669

FCE/ehm
Attachment: Request for Continued Prosecution Transmittal Form

J:\TPNT200XC1\PTO\Pre-Amdt.doc/DNB/ehm

TO:Auto-reply fax to 352 372 5800 COMPANY:

Auto-Reply Facsimile Transmission

TO: Fax Sender at 352 372 5800

Fax Information
Date Received: 2/9/2004 3:30:38 PM [Eastern Standard Time]
Total Pages: 17 (Including cover page)

ADVISORY: This is an automatically generated return receipt confirmation of the facsimile transmission received by the Office. Please check to make sure that the number of pages listed as received in Total Pages above matches what was intended to be sent. Applicants are advised to retain this receipt in the unlikely event that proof of this facsimile transmission is necessary. Applicants are also advised to use the certificate of facsimile transmission procedures set forth in 37 CFR 1.8(a) and (b), 37 CFR 1.6(f). Trademark Applicants, also see the Trademark Manual of Examining Procedure (TMEP) section 306 et seq.

Received Cover Page ==========>

FEB-08-2004 MON 03:18 PM SALIWANCHIK,LLOYD&SALIWA FAX NO. 352 372 5800 P. 01

FACSIMILE COVER SHEET

SALIWANCHIK, LLOYD & SALIWANCHIK
A Professional Association
2421 N.W. 41st Street
Suite A-1
Gainesville, FL 32606

Telephone (352) 375-8100
Facsimile (352) 372-5800

TO:	Examiner Maurie C. Baker	FROM:	Frank C. Eisenschenk, Ph.D. (Reg. No. 45,332)
COMPANY:	U.S. Patent & Trademark Office Art Unit 1639	DATE:	February 5, 2004
FAX NO.:	(703) 872-9306	NO. OF PAGES (INCLUDING COVER SHEET):	25

SUBJECT/MESSAGE: U.S. Patent Application Docket No. TPI-T200XC1
High-Throughput Formation, Identification and Analysis of Diverse Solid Forms
(Cima et al.)
Serial No. : 09/756,092
Filed : January 8, 2001
Conf. No. : 5650

ATTACHMENTS: Request for Continued Prosecution (1 Sheet)
Preliminary Amendment (23 Sheets)

THIS IS AN OFFICIAL DOCUMENT.
PLEASE DELIVER IMMEDIATELY. Thank you.

If you do not receive all pages or if any transmission is not legible, call the sender at (352) 375-8100.

PAGE 1/17 * RCVD AT 2/9/2004 3:30:38 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:8729306 * CSID:352 372 5800 * DURATION (mm-ss):03-52

TO:Auto-reply fax to 352 372 5800 COMPANY:

Auto-Reply Facsimile Transmission

TO: Fax Sender at 352 372 5800

Fax Information
Date Received: 2/9/2004 3:40:07 PM [Eastern Standard Time]
Total Pages: 10 (including cover page)

ADVISORY: This is an automatically generated return receipt confirmation of the facsimile transmission received by the Office. Please check to make sure that the number of pages listed as received in Total Pages above matches what was intended to be sent. Applicants are advised to retain this receipt in the unlikely event that proof of this facsimile transmission is necessary. Applicants are also advised to use the certificate of facsimile transmission procedures set forth in 37 CFR 1.8(a) and (b), 37 CFR 1.6(f). Trademark Applicants, also see the Trademark Manual of Examining Procedure (TMEP) section 306 et seq.

Received
Cover
Page
=======>

FEB-09-2004 MON 03:27 PM SALIWANCHIK,LLOYD&SALIWA FAX NO. 352 372 5800 P. 01

FACSIMILE COVER SHEET

SALIWANCHIK, LLOYD & SALIWANCHIK
A Professional Association
2421 N.W. 41st Street
Suite A-1
Gainesville, FL 32606

Telephone (352) 375-8100
Facsimile (352) 372-5800

TO: Examiner Maurie G. Baker
FROM: Frank C. Eisenschenk, Ph.D. (Reg. No. 45,332)
COMPANY: U.S. Patent & Trademark Office Art Unit 1639
DATE: February 9, 2004
FAX NO.: (703) 872-9306
NO. OF PAGES: (INCLUDING COVER SHEET) ~~27~~ 10

SUBJECT/MESSAGE: U.S. Patent Application Docket No. TPI-T200XC1
High-Throughput Formation, Identification and Analysis of Diverse Solid Forms
(Cima et al.)
Serial No. : 09/756,092
Filed : January 8, 2001
Conf. No. : 5630

ATTACHMENTS: Request for Continued Prosecution (1 Sheet)
Preliminary Amendment (21 Sheets) ——> p. 15-25

(Continued – following fax jam)

THIS IS AN OFFICIAL DOCUMENT.
PLEASE DELIVER IMMEDIATELY. Thank you.

[illegible]

If you do not receive all pages or if any transmission is not legible, call the sender at (352) 375-8100.

PAGE 1/10 * RCVD AT 2/9/2004 3:40:07 PM [Eastern Standard Time] * [illegible]